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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/767,041	01/22/2001	Hilda E. Smith	4726US	3344

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EXAMINER	
DUFFY, PATRICIA ANN	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 08/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/767,041	SMITH, HILDA E.	
	Examiner	Art Unit	
	Patricia A. Duffy	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *5-26-05 and 1-27-05*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18,21-25,32,33,38,50 and 53-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18,21-25,32,33,38,50 and 53-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1-27-05 has been entered.

Claims 1-17, 19-20, 26-31, 34-37, 39-49, 51-52 and 56-57 have been canceled. Claims 18, 21-25, 32, 33, 38, 50 and 53-55 are pending and under examination.

Requirement for Information

Applicant and the assignee of this application are required under 37 CFR 1.105 to provide the following information that the examiner has determined is reasonably necessary to the examination of this application.

In response to this requirement, please provide a copy of each of the following item of art referred to in the disclosure at page 13 paragraph [0046], Smith, ID-DLO-Annual Report 1996. It is noted that the specification teaches that this reference, Authored by Applicant and not submitted on any previous IDS of record, is relevant to the examination of the claimed invention because it allegedly discloses mutants of *Streptococcus suis* generated by homologus recombination or transposon mutagenesis.

Election/Restrictions

Specie SEQ ID NO:29, 37 and 43 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 5-26-05. Applicant's arguments have been carefully considered but are not persuasive. Applicants argue that there is no statutory section set forth in the requirement. Applicants are well aware that the statutory requirement for

species election is 35 USC 1.121. Applicants are directed to the MPEP "Nucleotide sequences encoding different proteins are structurally distinct chemical compounds and are unrelated to one another. These sequences are thus deemed to normally constitute independent and distinct inventions within the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such nucleotide sequence is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141 et seq.". Further, the claims are not directed to nucleic acid sequences per se, but a microorganism. There is no specific requirement that 10 different microorganims be examined. Further, as explained in the OG notice, the requirement was directed towards EST sequences. Finally, Applicants own specification indicates that genes are not structurally related to others, or to each other. As such, the each species requires a different search; can hold a separate patent and the requirement for a species election is maintained. Applicants have not stated that the sequences are obvious variants and as such, they are deemed to constitute independent and distinct inventions within the meaning of 35 U.S.C 121.

The species requirement is maintained.

Rejections Withdrawn

The rejection of claims 52-55 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is withdrawn in view of the cancellation or amendment to the claims.

The rejection of claims 15, 18, 21-25, 32, 33, 35-40, 50-57 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is withdrawn in view of the amendment to the claims.

The advisory that should claims 21-23, and 39 be found allowable, claims 35-37 and 39 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof is withdrawn based on the cancellation of the conflicting claims.

The rejection of claims 15, 18, 21-25, 32, 33, 35-40, 50-57 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the amendment to the claims.

Rejections Maintained

Claims 18, 21, 22, 23, 24, 25, 32, 33, 38, 50 and 55 stand rejected under 35 U.S.C. 102(b) as being clearly anticipated by Charland et al (Microbiology, 144:325-332, February 1998, of record on 1449) is maintained for reasons made of record in the Office Action mailed 1-20-04 and 9-16-04.

Charland et al teach two Streptococcus suis serotype 2 mutants deficient in capsular expression wherein the mutants are derived by transposition TN916 insertion from Enterococcus faecalis (see page 326, columns 1-2, in Methods). The *S. suis* mutants expressed the heterologous gene of the TN916 insertion from Enterococcus faecalis coding for tetracycline resistance. The mutants were selected based on the expression of streptomycin and tetracycline resistance. As such, the mutants of Charland et al expressed a heterologous protein from the pathogen *Enterococcus faecalis*. Both mutants were otherwise biochemically identical to the wild-type strain in that the production of the other putative virulence factors of S. suis such as haemolysin, MRP and EF were not

affected by transposition (page 327, paragraph bridging columns 1-2). The properties of "capable of survival" in an immune-competent host are inherent properties of the capsule-deficient mutants. The microorganisms were placed in growth broth comprising water, a pharmaceutically acceptable carrier (page 327, column 1, phagocytic assays and virulence assays and bacterial clearance test).

Applicants' arguments have been carefully considered but are not persuasive. Applicants argue that the prior art does not teach a mutation in the claimed sequences. This is not persuasive; the sequences are inherent to the prior art. Further, the claims do not require that the mutation in the sequence specifically induce capsular deficiency. Therefore, the mutation causing capsular deficiency may lie outside of the recited nucleic acid sequence. Further, the claims as currently drafted specifically encompass unlimited naturally occurring variation of SEQ ID NO:9. Therefore, the art still meets all the limitation of the claimed invention. Since the *S. suis* serotype 2 strain of the prior art is different from serotype 2 strain 10 from which the serotype 2 genes were cloned, it appears that the *S. suis* acapsular mutant of the art is a mutant or variant of SEQ ID NO:9, absent factual evidence to the contrary.

Since the Office does not have the facilities for examining and comparing applicant's protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the structural and functional characteristics of the claimed mutant). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald* et al., 619 F.2d 67, 205 USPQ 594 (CCPA 1980).

New Rejections Based on Amendment

Applicant is advised that should claim 24 be found allowable, claim 55 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims

in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claims 18, 21-25, 32, 33, 38, 53 and 55 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to a *Streptococcus suis* mutant deficient in capsular expression, wherein the *Streptococcus suis* mutant comprises a mutation in the sequence selected from the group consisting of SEQ ID NO:9, SEQ ID NO:29, SEQ ID NO:37 and SEQ ID NO:43 and a pharmaceutically acceptable carrier or adjuvant. Applicant has specifically removed the language that the mutation causing the deficiency is in the recited sequence and as such, the claims currently read on any acapsular serotype 2 strain variant. It is noted that the sequences were derived from *S. suis* serotype 2, strain 10 (page 23 paragraph [00120]). The teachings of the specification are limited to two specific deletion mutations wherein a part of the *cps2B* gene of was replaced by the streptomycin-resistance gene (mutant 10cpsB) and the 3' end of the *cps2E* gene as well as the 5' end of the *cps2F* gene were placed by the streptomycin-resistance gene (mutant 10cpsEF; see marked up specification [00159]). The deletions were made using nucleic acid sequence data obtained from the cloning of the particular genes from *S. suis* serotype 2, strain 10. The teachings of the specification are limited to disruption of these two specific genes in *S. suis* and provides for a phenotype of a mutant with deficient capsular expression. The current claims encompass any mutation anywhere in the entire *S. suis*

genome that provides for a mutant with a phenotype with deficient capsular expression. The term "mutant" is seen to encompass insertions, deletions, point mutations, and inversions of particular sequences (see marked up specification [0047-0048]) and as currently constructed, naturally occurring variants of the CPS2 gene cluster from different strains. The specification does not disclose any mutation outside of the particularly disclosed genes *cps2B* , *cps2E, cps2F* , that when disrupted provide for a mutant with a phenotype of deficient capsular expression. The disruption of 3 particular genes having particular sequences within an entire genome having a multitude of undisclosed and undescribed genes that may or may not impact capsular expression does not provide adequate written description support for the broad genus now claimed. Applicants own specification teaches that *S. suis* has at least 35 different serotypes and is remarkably heterogeneous. The specification teaches that many of the cloned serotype 2 genes are not conserved in the other 34 species of *S. suis* (see Table 4, page 134 of marked up specification). Similar findings were presented for serotypes 1 and 9 (Table 5, pages 135-136). Therefore, the teachings of the two serotype 2 deletion mutants using specific nucleotide sequences of specific genes does not provide description of the genus which is highly variant and includes loci outside of the particularly cps cloned genes described in the specification. The specification lacks written description of mutants and gene loci from a representative number of serotypes of *S. suis* that when mutated provide for the requisite deficient capsular expression. The claims specifically encompass mutations by homologous recombination in loci outside of the particularly cloned cps loci. The specification fails to describe a single locus outside of the particularly cloned cps loci that would necessarily produce mutants as claimed. There is no characterization of such mutants and the specification describes none. The specification does not place any structure or chemical limitations on the mutants. The recitation of mutant deficient in capsular expression does not convey a common structure or function because the term deficient is described in the specification at [0045] and it is clear from this description

that the term "deficient" does not provide similar structure or function. The term deficient includes no capsule, organization of the capsular material has been rearranged and others that have a nearly fully developed capsule that is only deficient in a particular sugar component. As such, the term deficient as it is recited in the claim does not and cannot provide a common structural or functional feature. The scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members are permitted. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description, because specific, not general guidance is needed. Since the disclosure fails to describe the common attributes or structural characteristics that identify members of the genus and because the genus is highly variant, the terms "mutant" and "deficiency in capsular expression" alone is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure of a two specific gene deletions (i.e. knock-outs) in a single serotype of *S. suis*, fails to provide a representative number of species describe the claimed genus when the single function genus is highly diverse. Applicants were not in possession of the claimed genus because the specification does not convey to one of skill in the art a representative number of variants in structure and function of any such mutants that have the claimed function of deficiency in capsular expression. The genus of polypeptides with the claimed function is substantial and highly variant because the polypeptides do not have a common structure and function. As such the specification lacks written description for the highly variant genus of single function mutants and one skilled in the art would not recognize that applicants had possession of the genus of claimed genus of *S. suis* mutants as instantly claimed.

Applicants' arguments in the response after final filed 1-27-05 have been carefully considered as they relate to the rejection set forth above, but are not persuasive. Applicants assert that they have taught how to make mutants because they have taught

the nucleic acid structure of specific gene. This is not persuasive, Applicants have taught how to make knock-out mutants of specifically delineated csp genes that provide for a capsular deficient phenotype and the claims are not so limited. Knock-out mutants do not provide written description of other mutants as defined in the specification to specifically encompass insertions, deletions, point mutations, and inversions of particular sequences (see marked up specification [0047-0048]). The specification lacks written description of the plethora of mutants contemplated by the specification. There is no description of insertions, point mutations or inversions as specifically set forth in the specification and embraced in the term mutant. Further, the claims as amended no longer require that the mutation of SEQ ID NO:9, 29, 37, and 43 provide for the claimed phenotype of capsular deficient. Applicants have unintentionally further broadened out the claimed invention. The current claim structure does not specify that the mutation in the sequence is responsible for the phenotype of capsular deficient. Description of a sequence does not provide for description of mutations of the sequence (i.e. point mutations, inversions or insertions) that are highly variant. As such, it is clear that the description of two-gene knock-outs in specific genes does not provide written description of the genus of mutants now claimed. The rejection is maintained for reasons made of record.

Claim 54 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As to claim 54, the claim recites "a" mutated cpsB, "a" mutated cpsEF gene or a combination thereof. "A" means any and therefore, lacks clear basis in claim 18. Further, the claim does not specify the metes and bounds of cps, cpsEF as it relates to any of the individually claimed sequences and as such, there is no clear antecedent basis in the claims and the skilled artisan would not know whether or not they were infringing on the claim or not.

Status of the Claims

All claims stand rejected.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 571-272-0855. The examiner can normally be reached on M-Th 6:30 am - 6:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patricia A. Duffy

Patricia A. Duffy, Ph.D.
Primary Examiner
Art Unit 1645

L. R. F. Smith

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